

REMARKS

Prior to the present reply, claims 42-48, 50-53, and 163-194 were pending. Due to a Restriction Requirement, claims 42-46, 48, 51-53, and 164-193 are withdrawn from consideration. In the final Office action mailed April 27, 2009, claims 47, 50, 163, and 194 are examined and have been rejected under 35 U.S.C. § 112, first paragraph, as failing to comply with the written description requirement. This rejection is addressed below.

Examiner interview

The undersigned thanks Examiner Teller for the helpful telephonic interview on August 5, 2009. During the interview, proposed amendments were presented. The written description rejection, in view of the amended claims, was discussed. Also discussed was the application of the restriction requirement to the pending claims.

Claim amendments

Claim 163 has been amended to require that j, k, and m are 0 and that l and n are 1. Claim 163 has also been amended to require that R_d and R_f are each the side chain of Gly. The amino acid side chains of R_g, R_h, and R_i, and R_j have also been amended. Finally, the structure shown in claim 163 has been amended to reflect these changes. Specifically, the

amino acids containing R_a, R_b, and R_c have been removed from the structure shown because j, k, and m are required to be 0.

New claim 195 also recites a structure based on Formula XII. In this structure, j, k, l, m, p, and q are required to be 0, R_d is required to be Ala or Gly, R_f is required to be Ala or Gly, and R_i is required to be Tyr. Support for this claim is found in formula XII, on pages 49 and 50 of the specification. Claim 196 recites that R_g is Asn. Support for this amendment is found, for example, at page 50, line 32. Claims 173-193 have been amended to depend from claim 195. These amendments add no new matter.

Application title

Applicants respectfully request entry of their amendment to the application title. Applicants amended the title of the application to recite “Novel Antiarrhythmic Peptides” both in the Reply to Restriction Requirement mailed November 27, 2006 and in a Supplemental Application Data Sheet filed with in conjunction with the Reply to Office Action mailed September 27, 2007. Action on this amendment is therefore respectfully requested.

The restriction requirement

Applicants respectfully request that all claims reading on the elected species be examined. In the Reply to Restriction Requirement mailed November 27, 2006,

Applicants elected Group II, directed to compounds of formula XII, and a species of cyclo-(Gly-Ala-Gly-Hyp-Pro-Tyr-Asn-) (Compound 36; SEQ ID NO:287) for examination.

Compound 36, the elected species, is recited in claim 165. The Office has indicated this claim as being withdrawn. Because this claim recites the elected species, this claim should be examined.

In addition, linking claims, such as generic claims, *must* be examined with, and are considered part of, the elected invention (see M.P.E.P. § 809). Thus generic claims that encompass the elected species, including withdrawn claims 42 and 51-53, should also be examined.

Rejection under 35 U.S.C. § 112, first paragraph

Claims 47, 50, 163, and 194 stand rejected under 35 U.S.C. § 112, first paragraph, as failing to comply with the written description requirement. Applicants respectfully traverse the rejection, as applied to the amended claims. In making this rejection, the Office asserts that numerous “L” forms of the formula are disclosed, but submits that the specification fails to provide sufficient descriptive information regarding the retro, all-D, and retro all-D forms of the formula. The Office further asserts that experimental data is provided only for compound 2 (SEQ ID NO:298) only.

As amended, claim 163 recites a genus encompassing peptides of 5-7 amino acids in length, as the amino acids containing side chains R_a , R_b , and R_e are required to absent and the amino acids containing side chains R_c and R_f are required to be present. Further, the side chains of amino acids l and n (i.e., R_c and R_f) are now each required to be Gly. R_d is required to be the side chain of Ala. Thus, all peptides of amended claim 163 have a “Gly-Ala-Gly” sequence.

Claim 163 has been further requires that R_g is one of ten different amino acid side chains, R_h is one of three different amino acid side chains, R_i is one of two different amino acid side chains (with one or more optional halogen substitutions), and R_j is one of two amino acid side chains.

Following these changes, claim 163 encompasses a genus of peptides represented by the formula:

X-Gly-Ala-Gly-X4-[Ala/Pro/D-Pro]-Tyr/D-Tyr-[Gln/Asn]-(OH/NH₂)
and pharmaceutically acceptable salts thereof, where X is H, Ac, TFa, DBF, ASAL (optionally iodinated), or HP, X4 is selected from among ten different amino acids and the “Tyr/D-Tyr” optionally has one or more halogen substitution in the aromatic ring. The amino acids present inside square brackets may be absent. The claim also encompasses cyclic forms of these peptides (where the C-terminal OH/NH₂ group is absent), as well as retro, all-D, and retro all-D forms of these compounds.

The specification discloses a representative number of species

The written description requirement can be satisfied through description of a representative number of species by actual reduction to practice. A “representative number of species” means that the species, which are adequately described, are representative of the entire genus. The peptides disclosed in the specification are both adequately described and representative of the entire genus of claim 163, as outlined below.

The specification describes synthesis of 22 peptides (Compounds 2, 3, 5-14, 22-26, and 35-39) that fall within the claimed genus. These compounds contain each amino acid substitution recited in claim 163. Linear and cyclic peptides are disclosed, as are “L” forms, retro forms, all-D forms, and retro all-D forms of the peptides of the formula recited in claim 163

Each of the described peptides has a “Gly-Ala-Gly” sequence. As R_c , R_d , and R_f are required to be the side chains Gly, Ala, Gly, respectively, these side chains are well described by the specification.

The remaining amino acid side chains recited in claim 163 are also exemplified by at least one peptide whose synthesis is described in the specification. For instance, R_g is selected from among ten different amino acid side chains. Each of these ten side chains is found in one or more of the peptides described in the specification; see, for example, compounds 3, 5, 6, 8, 11-14, 37, and 39. Similarly, R_h is selected from the side chains of

Pro, Ala, and D-Pro. These side chains are found, for example, in compounds 6-8. R_i is selected from the side chains of Tyr and D-Tyr, optionally having one or more halogen substitutions. These side chains, both substituted and unsubstituted, are found, for example, in Compounds 2, 3, 24, and 38. Finally, R_j is selected from the side chains Gln and Asn. These side chains are found, for example, in Compounds 35 and 36.

The formula of claim 163 also includes peptides where one or both of amino acids p and q (which contain the side chains R_h and R_j) are absent. Such peptide include Compounds 2, 5-14, 22, 24-26, and 39.

Claim 163 includes linear and cyclic peptides, both of which are described in the application. Compounds 2, 5-14, 22-26, and 39 are linear, and Compounds 3 and 35-38 are cyclic.

Finally, Claim 163 includes retro, all-D, and retro all-D peptides. Retro compounds include compound 2, 3, 24-26, and 38. "All-D" compounds include 2 and 22-26. "Retro all-D" compounds include Compounds 2 and 24-26.

Thus, each amino acid substitution recited in claim 163 is exemplified by one or more peptides. Linear and cyclic peptides are disclosed, as are a substantial number of retro, all-D, and retro all-D peptides. The peptides described in the specification thus are representative of the entire genus of claim 163.

A substantial number of claimed compounds possess antiarrhythmic activity

The Office asserts that data is provided for Compound 2 only and that the same results from two different peptides cannot be expected, absent experimental evidence. On this point, Applicants respectfully direct the Office's attention to pages 79-82 of the specification. Here, test results from an in vivo mouse antiarrhythmic activity assay are described. This assay uses a CaCl_2 injection to induce arrhythmia in anesthetized mice. Delay of arrhythmia onset upon administration of a compound of the invention in conjugation with a CaCl_2 injection was measured as a test of antiarrhythmic activity. In this assay, Compounds 2, 3, 5, 9, 10, 12, 14, 35, 36, and 39 were tested and each of these compounds was found to have antiarrhythmic activity. Thus, experimental data is provided for a substantial number of compounds encompassed by the claimed genus, thus demonstrating Applicants' possession of the claimed peptides. For this reason as well, claim 163 and its dependent claims comply with the written description requirement.

For the reasons set for the above, withdrawal of the rejection under § 112, first paragraph, of claim 163 and its dependent claims is respectfully requested.

New claims 195 and 196 are also described by the specification

Applicants also present a genus that encompasses 3-4 amino acid peptides, based on formula XII. This genus of peptides can be represented as follows:



where X is any amino acid (with certain exceptions) and the amino acid in square brackets is optionally present. The claim also includes the retro, all-D, and retro all-D forms of this formula. These peptides are exemplified in the specification by compounds 40-43, which are three and four amino acid peptides having the sequences H/Ac-G-N-Y-NH₂ and H/Ac-A-G-N-Y-NH₂. These peptides provide a representative number of species of the claimed peptides of claims 195 and 196. Applicants submit that these claims, as well as dependent claims 173-196 likewise comply with the written description requirement.

CONCLUSION

Applicants submit that the claims are in condition for allowance and that such action is respectfully requested. Enclosed is a Petition to extend the period for replying to the final Office action for one (1) month, to and including August 27, 2009.

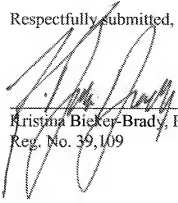
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Respectfully submitted,

Date:

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